WEST Search History

DATE: Wednesday, June 25, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L16	l13 and antibacterial	45	L16
L15	L14 and antimicrobial	51	L15
L14	L13 and (bacteri$ or cancer or fungal)	80	L14
L13	L12 and cecropin adj3 magainin	83	L13
L12	L9 and (hybrid or fusion)	198	L12
L11	l9 and (hybrid or fusion or fusing)	199	L11
L10	L9 and (hybrid or fusi$)	206	L10
L9	cecropin and magainin	326	L9
L8	ca-ma peptide	1	L8
L7	ca-ma	8	L7
L6	l1 or l2 or l3 or l4 or L5	5	L6
L5	hahm-h.in.	4	L5
L4	hahm-hyung-soo.in.	0	L4
L3	kim-hyung-heun.in.	0	L3
L2	lee-dong-gun.in.	1	L2
L1	park-yoonkyung.in.	1	L1

END OF SEARCH HISTORY

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 95960

TO: Nita M Minnifield
Location: cm1/8a07/8e12
Art Unit: 1645

6/10/03
Case Serial Number: 081418

From: Toby Port
Location: Biotech-Chem Library
CM1-6A04
Phone: 308-3534

toby.port@uspto.gov

Search Notes

(9) Modified cecropin A-magainin2 peptide
hydrophilic aa substituted w/ hydrophobic aa

(10) SEQ 1, residues 9, 10 " → now pro
" 4, 8, 14, 15 → " lys
" 5, 6, 12, 13, 16, 17 → leucine

(11) SEQ 2

```
=> file caplus; d que 15
FILE 'CAPLUS' ENTERED AT 15:53:16 ON 10 JUN 2003
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FILE COVERS 1907 - 10 Jun 2003  VOL 138 ISS 24
FILE LAST UPDATED: 9 Jun 2003  (20030609/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1          171 SEA FILE=CAPLUS ABB=ON  PLU=ON  HAHM K?/AU
L2         9493 SEA FILE=CAPLUS ABB=ON  PLU=ON  LEE D?/AU
L3         6802 SEA FILE=CAPLUS ABB=ON  PLU=ON  PARK Y?/AU
L4        18572 SEA FILE=CAPLUS ABB=ON  PLU=ON  KIM H?/AU
L5            8 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1 AND L2 AND L3 AND L4
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=> file medline; d que l30
FILE 'MEDLINE' ENTERED AT 15:54:03 ON 10 JUN 2003
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FILE LAST UPDATED: 8 JUN 2003 (20030608/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L30           4 SEA FILE=MEDLINE ABB=ON  PLU=ON  HAHM K?/AU AND LEE D?/AU AND
                PARK Y?/AU AND KIM H?/AU
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=> file embase; d que l34
FILE 'EMBASE' ENTERED AT 15:54:11 ON 10 JUN 2003
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FILE COVERS 1974 TO 5 Jun 2003 (20030605/ED)

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L34             1 SEA FILE=EMBASE ABB=ON  PLU=ON  HAHM K?/AU AND LEE D?/AU AND
                  PARK Y?/AU AND KIM H?/AU


=> file wpix; d que l50
FILE 'WPIX' ENTERED AT 15:54:21 ON 10 JUN 2003
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FILE LAST UPDATED:          9 JUN 2003      <20030609/UP>
MOST RECENT DERWENT UPDATE:     200336        <200336/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> SLART (Simultaneous Left and Right Truncation) is now
    available in the /ABEX field. An additional search field
    /BIX is also provided which comprises both /BI and /ABEX <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L50             2 SEA FILE=WPIX ABB=ON  PLU=ON  HAHM K?/AU AND LEE D?/AU AND
                  PARK Y?/AU AND KIM H?/AU


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FILE 'MEDLINE' ENTERED AT 15:54:36 ON 10 JUN 2003

FILE 'CAPLUS' ENTERED AT 15:54:36 ON 10 JUN 2003
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PROCESSING COMPLETED FOR L30
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L50
L55            10 DUP REM L30 L5 L34 L50 (5 DUPLICATES REMOVED)
                  ANSWERS '1-4' FROM FILE MEDLINE
                  ANSWERS '5-8' FROM FILE CAPLUS
                  ANSWERS '9-10' FROM FILE WPIX

=> d ibib ab l55 1-10
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L55 ANSWER 1 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003223670 IN-PROCESS
DOCUMENT NUMBER: 22630154 PubMed ID: 12745074
TITLE: Fungicidal effect of indolicidin and its interaction with phospholipid membranes.
AUTHOR: **Lee Dong Gun; Kim Hyung Keun;** Kim Sun Am; **Park Yoonkyung;** Park Seong Cheol; Jang Seung Hwan; **Hahm Kyung Soo**
CORPORATE SOURCE: School of Life Science and Biotechnology, College of Natural Sciences, Kyungpook National University, 1370 Sankyuk-dong, Puk-ku, 702-701, Taegu, Republic of Korea.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2003 May 30) 305 (2) 305-10.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030515
Last Updated on STN: 20030515

AB The fungicidal effect and mechanism of a tryptophan-rich 13-mer peptide, indolicidin derived from granules of bovine neutrophils, were investigated. Indolicidin displayed a strong fungicidal activity against various fungi. In order to understand the fungicidal mechanism(s) of indolicidin, we examined the interaction of indolicidin with the pathogenic fungus Trichosporon beigelii. Fluorescence confocal microscopy and flow cytometry analysis revealed that indolicidin acted rapidly on the plasma membrane of the fungal cells in an energy-independent manner. This interaction is also dependent on the ionic environment. Furthermore, indolicidin caused significant morphological changes when tested for the membrane disrupting activity using liposomes (phosphatidylcholine/cholesterol; 10:1, w/w). The results suggest that indolicidin may exert its fungicidal activity by disrupting the structure of cell membranes; via direct interaction with the lipid bilayers, in a salt-dependent and energy-independent manner.

L55 ANSWER 2 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002131562 MEDLINE
DOCUMENT NUMBER: 21855933 PubMed ID: 11866466
TITLE: Antifungal mechanism of an antimicrobial peptide, HP (2--20), derived from N-terminus of Helicobacter pylori ribosomal protein L1 against Candida albicans.
AUTHOR: **Lee Dong Gun; Park Yoonkyung; Kim Hee Nam; Kim Hyung Keun;** Kim Pyoung Il; Choi Bo Hwa; **Hahm Kyung-Soo**
CORPORATE SOURCE: Research Center for Proteineous Materials, Chosun University, 375 Seosuk-Dong, Dong-Ku, Kwangju 501-759, Korea.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2002 Mar 8) 291 (4) 1006-13.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020228
Last Updated on STN: 20020416
Entered Medline: 20020415

AB The antifungal activity and mechanism of HP (2-20), a peptide derived from

the N-terminus sequence of Helicobacter pylori Ribosomal Protein L1 were investigated. HP (2--20) displayed a strong antifungal activity against various fungi, and the antifungal activity was inhibited by Ca(2+) and Mg(2+) ions. In order to investigate the antifungal mechanism(s) of HP (2-20), fluorescence activated flow cytometry was performed. As determined by propidium iodide staining, Candida albicans treated with HP (2-20) showed a higher fluorescence intensity than untreated cells and was similar to melittin-treated cells. The effect on fungal cell membranes was examined by investigating the change in membrane dynamics of C. albicans using 1,6-diphenyl-1,3,5-hexatriene as a membrane probe and by testing the membrane disrupting activity using liposome (PC/PS; 3:1, w/w) and by treating protoplasts of C. albicans with the peptide. The action of peptide against fungal cell membrane was further examined by the potassium-release test, and HP (2-20) was able to increase the amount of K(+) released from the cells. The result suggests that HP (2-20) may exert its antifungal activity by disrupting the structure of cell membrane via pore formation or directly interacts with the lipid bilayers in a salt-dependent manner.

L55 ANSWER 3 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002398239 MEDLINE
DOCUMENT NUMBER: 22142243 PubMed ID: 12147359
TITLE: Design of novel analogue peptides with potent antibiotic activity based on the antimicrobial peptide, HP (2-20), derived from N-terminus of Helicobacter pylori ribosomal protein L1.
AUTHOR: **Lee Dong Gun; Kim Hee Nam; Park Yoonkyung; Kim Hyung Keun;** Choi Bo Hwa; Choi Cheol-Hee; **Hahm Kyung-Soo**
CORPORATE SOURCE: Research Center for Proteineous Materials, Chosun University, 375 Seosuk-Dong, Dong-Ku, Kwangju, South Korea.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (2002 Jul 29) 1598 (1-2) 185-94.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020731
Last Updated on STN: 20021012
Entered Medline: 20021011

AB HP (2-20) (AKKVFKRLEKLFSKIQNDK) is the antimicrobial sequence derived from the N-terminus of Helicobacter pylori ribosomal protein L1 (RPL1). In order to develop novel antibiotic peptides useful as therapeutic agents, potent antibiotic activities against bacteria, fungi and cancer cells without a cytotoxic effect are essential. To this end, several analogues with amino acid substitutions were designed to increase or decrease only the net hydrophobicity. In particular, the substitution of Trp for the hydrophobic amino acids, Gln and Asp at positions 17 and 19 of HP (2-20) (Anal 3), caused a dramatic increase in antibiotic activity without a hemolytic effect.In contrast, the decrease of hydrophobicity brought about by substituting Ser for Leu and Phe at positions 12 and 19 of HP (2-20), respectively (Anal 4, Anal 5), did not have a significant effect on the antibiotic activity. The antibiotic effects of these synthetic peptides were further investigated by treating prepared protoplasts of Candida albicans and conducting an artificial liposomal vesicle (PC/PS; 3:1, w/w) disrupting activity test. The results demonstrated that the Anal 3 prevented the regeneration of fungal cell walls and induced an enhanced release of fluorescent dye (carboxyfluorescein) trapped in the artificial membrane vesicles to a greater degree than HP (2-20).The potassium-release

test conducted on C. albicans indicated that Anal 3 induced greater amounts of potassium ion to be released than the parent peptide, HP (2-20) did. These results indicated that the hydrophobic region of peptides is prerequisite for its effective antibiotic activity and may facilitate easy penetration of the lipid bilayers of the cell membrane.

L55 ANSWER 4 OF 10 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001332529 MEDLINE
DOCUMENT NUMBER: 21294772 PubMed ID: 11401498
TITLE: Fungicidal effect of antimicrobial peptide, PMAP-23, isolated from porcine myeloid against Candida albicans.
AUTHOR: **Lee D G**; Kim D H; **Park Y**; **Kim H K**; **Kim H N**; Shin Y K; Choi C H; **Hahm K S**
CORPORATE SOURCE: Research Center for Proteineous Materials, Department of Pharmacology, School of Medicine, Chosun University, 375 Seosuk-Dong, Kwangju, Dong-Ku, 501-759, Korea.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Mar 30) 282 (2) 570-4.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB The antifungal activity and mechanism of a 23-mer peptide, PMAP-23, derived from pig myeloid was investigated. PMAP-23 displayed strong antifungal activity against yeast and mold. To investigate the antifungal mechanism of PMAP-23, fluorescence activated flow cytometry and confocal laser scanning microscopy were performed. Candida albicans treated with PMAP-23 showed higher fluorescence intensity by propidium iodide(PI) staining, which was similar to that of Melittin than untreated cells. Confocal microscopy showed that the peptide was located in the plasma membrane. The action of peptides against fungal cell membranes was examined by treating prepared protoplasts of C. albicans with the peptide and lipid vesicle titration test. The result showed that the peptide prevented the regeneration of fungal cell walls and induced release of the fluorescent dye trapped in the artificial membrane vesicles, indicating that the peptide exerts its antifungal activity by acting on the plasma lipid membrane.

L55 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:396440 CAPLUS
TITLE: Novel anticancer and antibiotic peptides with increased positive charge and hydrophobicity made by substituting one or more amino acids of cecropin A-magainin 2 (CA-MA) peptide and their pharmaceutical compositions
INVENTOR(S): **Hahm, Kyung-soo**; **Lee, Dong Gun**; **Park, Yoonkyung**; **Kim, Hee Nam**
PATENT ASSIGNEE(S): S. Korea
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003096745	A1	20030522	US 2002-81418	20020222

PRIORITY APPLN. INFO.: KR 2001-57837 A 20010919

AB The present invention relates to novel peptides with increased + charge and hydrophobicity by substituting one or more amino acids of CA-MA peptide in which cecropin A (CA) and magainin 2 (MA) were conjugated and pharmaceutical compns. contg. thereof. More precisely, the present invention relates to synthetic peptides prepd. by substituting one or more amino acids of CA-MA peptide represented by the sequence Lys-Trp-Lys-Leu-Phe-Lys-Lys-Ile-Gly-Ile-Gly-Lys-Phe-Leu-His-Ser-Ala-Lys-Lys-Phe with amino acids having + charge and hydrophobicity and anti-bacterial, anti-fungal and anticancer compns. contg. thereof. The synthetic peptides of the present invention have no cytotoxicity but have excellent anti-bacterial, anti-fungal and anticancer activity, leading in an effective use thereof as a safe anticancer agent and antibiotics.

L55 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:833794 CAPLUS
DOCUMENT NUMBER: 138:150123
TITLE: Antimicrobial mechanism of .beta.-glycyrrhetinic acid isolated from licorice, Glycyrrhiza glabra
AUTHOR(S): **Kim, Hyung Keun; Park, Yoonkyung; Kim, Hee Nam**; Choi, Bo Hwa; Jeong, Hye Gwang; **Lee, Dong Gun; Hahm, Kyung-Soo**
CORPORATE SOURCE: Research Center for Proteineous Materials, Chosun University, Kwangju, 501-759, S. Korea
SOURCE: Biotechnology Letters (2002), 24(22), 1899-1902 CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .beta.-Glycyrrhetinic acid isolated from Glycyrrhiza glabra had an antibacterial activity of 7.6 and 12.5 .mu.g ml-1 against Bacillus subtilis and Staphylococcus epidermidis without causing hemolysis of human erythrocytes, whereas it was not inhibitory against Escherichia coli, Proteus vulgaris and various fungi. Confocal microscopy showed that .beta.-glycyrrhetinic acid was located within the bacteria but had not caused membrane disruption. It then inhibited synthesis of DNA, RNA and protein.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:500410 CAPLUS
DOCUMENT NUMBER: 137:322456
TITLE: Importance of the length of the N- and C-terminal regions of Helicobacter pylori ribosomal protein L1 (RPL1) on its antimicrobial activity
AUTHOR(S): **Park, Yoonkyung; Lee, Dong Gun; Kim, Hee Nam; Kim, Hyung Keun**; Woo, Eun-Rhan; Choi, Cheol-Hee; **Hahm, Kyung-Soo**
CORPORATE SOURCE: School of Medicine, Research Center for Proteineous Materials (RCPM), Chosun University, Dong-Ku, Kwangju, 501-759, S. Korea
SOURCE: Biotechnology Letters (2002), 24(14), 1209-1215 CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HP (2-20) (AKKVFKRLEKLFSKIQNDK-NH2) is an antibacterial 19-mer peptide derived from the N-terminal region of Helicobacter pylori ribosomal protein L1 (RPL1). Several truncated peptides were synthesized to investigate the effects of the N- or C-terminal regions of HP (2-20) on antimicrobial activity. The antimicrobial activity of the peptides was measured by their growth inhibitory effect upon Pseudomonas aeruginosa, Salmonella typhimurium, Saccharomyces cerevisae, Trichosporon beigelii and Candida albicans. Antimicrobial activity required a full length N-terminus. None of the peptides exhibited hemolytic activity against human erythrocyte cells. The membrane-disrupting activity of these peptides, using liposomes and 1,6-diphenyl-1,3,5-hexatriene (DPH) as a probe, confirmed that the full N-terminal region of HP (2-20) is a prerequisite for antibiotic activity and that this region may facilitate penetration of the cell membrane. CD indicated that the .alpha.-helical structure of the peptides important for antimicrobial activity.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:289191 CAPLUS
DOCUMENT NUMBER: 137:30445
TITLE: Antibacterial activities of peptides designed as hybrids of antimicrobial peptides
AUTHOR(S): **Kim, Hyung Keun; Lee, Dong Gun; Park, Yoonkyung; Kim, Hee Nam**; Choi, Bo Hwa; Choi, Cheol-Hee; **Hahm, Kyung-Soo**
CORPORATE SOURCE: Research Center for Proteineous Materials (RCPM), Chosun University, Kwangju, 501-759, S. Korea
SOURCE: Biotechnology Letters (2002), 24(5), 347-353
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hybrid peptides (HP-MA, HP-ME), each of 20 residues and incorporating 2-9 residues of Helicobacter pylori ribosomal protein L1 (HP) and 1-12 residues of magainin 2 and melittin, were designed. The antibiotic activities of these peptides were evaluated using bacterial, tumor and human erythrocyte cells. HP-MA had a stronger antibacterial activity against Gram-pos. bacteria and Gram-neg. bacteria than HP (2-20) and magainin 2, and HP-ME was similar to melittin. None of the hybrids had anti-tumor or hemolytic activity. These peptides were further investigated using an artificial liposomal vesicle and 1,6-diphenyl-1,3,5-hexatriene as a membrane probe, and confirmed to have similar antibacterial activities. The antibacterial effect of these hybrids is probably caused by their ability to damage the bacterial plasma membrane. Addnl. CD spectra suggested that the .alpha.-helical structure of these peptides plays an important role in their antibiotic effect but that .alpha.-helical property is less connected with the enhanced antibiotic activity.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 9 OF 10 WPIX (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2003-207713 [20] WPIX
DOC. NO. CPI: C2003-052809
TITLE: New antifungal peptide and its use.
DERWENT CLASS: B04
INVENTOR(S): CHAE, S O; CHOI, B H; CHOI, J S; **HAHM, K S; KIM, H G; KIM, H N**; KIM, M J; KIM, P I; **LEE, D G; PARK, Y G**
PATENT ASSIGNEE(S): (HAHM-I) HAHM K S; (LEED-I) LEE D G

COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 2002082658	A	20021031	(200320)*		1

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 2002082658	A	KR 2001-22371	20010425

PRIORITY APPLN. INFO: KR 2001-22371 20010425
AB KR2002082658 A UPAB: 20030324
NOVELTY - Peptide described in sequence number 1 derived from pig's myeloid and the use thereof as an antifungal agent are provided. Therefore, the peptide shows excellent antifungal activity against pathogenic fungus, is not cytotoxic to human cells and can be effectively used as a safe peptide clinical pharmaceutical formulation.
DETAILED DESCRIPTION - An antifungal agent contains peptide described in sequence number 1 as an effective ingredient and exhibits excellent antifungal activity against pathogenic fungus, in particular Candida albicans(TIMM 1768), Trichosporon beigelii(KCTC 7707), Saccharomyces cerevisiae(KCTC 7296) and Trichophyton rubrum. The peptide acts on a lipid component of a cell membrane.
Dwg.1/10

L55 ANSWER 10 OF 10 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-207569 [20] WPIX
DOC. NO. CPI: C2003-052796
TITLE: Novel synthetic antibacterial hybrid peptide derived from ribosomal protein L1 of helicobacter pylori and use.
DERWENT CLASS: B04
INVENTOR(S): CHAE, S O; CHOI, B H; **HAHM, K S; KIM, H G; KIM, H N**; KIM, M J; **LEE, D G; PARK, Y G**
PATENT ASSIGNEE(S): (HAHM-I) HAHM K S; (LEED-I) LEE D G
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 2002074610	A	20021004	(200320)*		1

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 2002074610	A	KR 2001-14488	20010321

PRIORITY APPLN. INFO: KR 2001-14488 20010321
AB KR2002074610 A UPAB: 20030324
NOVELTY - Provided is a novel synthetic antibacterial hybrid peptide derived from Ribosomal Protein L1 of Helicobacter pylori and the use thereof. The synthetic antibacterial hybrid peptide has excellent antifungal and antibacterial activities without toxicity to remove bacteria which show antibiotics resistance.
DETAILED DESCRIPTION - The synthetic antimicrobial hybrid peptide is

manufactured by hybridizing the amino terminal region of RPL1(ribosomal protein L1) protein produced by Helicobacter pylori with the amino terminal regions of melittin and magainin. The amino terminal region of RPL1(ribosomal protein L1) protein is represented by the SEQ ID NO:1, and the amino terminal regions of melittin and magainin are represented by SEQ ID NO:2 and SEQ ID NO:3 respectively.
Dwg.1/10

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=> file hcaplus; d que l21; d que l27; d que l28
FILE 'HCAPLUS' ENTERED AT 15:55:16 ON 10 JUN 2003
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FILE COVERS 1907 - 10 Jun 2003 VOL 138 ISS 24
FILE LAST UPDATED: 9 Jun 2003 (20030609/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L6       108913 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEPTIDES/CT
L16           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CA-MA PEPTIDE
L21           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L16


L6       108913 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEPTIDES/CT
L7         7889 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIMICROBIAL AGENTS+OLD/CT
L8        46633 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BACTERICIDES/CW
L9       155938 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMOR AGENTS+PFT/CT
L10       69088 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FUNGICIDES+PFT/CT
L11        8927 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYDROPHOBICITY+PFT/CT
L12        7889 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIMICROBIAL AGENTS/CT
L13       23395 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ELECTRIC CHARGE/CT
L15         586 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MAGAININ
L19         227 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CECROPIN A
L20          33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L19 AND L15
L27          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND (L7 OR L8 OR L9 OR
                L10 OR L11 OR L12 OR L13)


L6       108913 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEPTIDES/CT
L15         586 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MAGAININ
L19         227 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CECROPIN A
L20          33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 AND L19 AND L15
L22       98904 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBACTERIAL AGENTS+OLD/CT
                OR ANTIBACTER?
L23       46633 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BACTERICIDES/CW
L24       88804 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BACTERICID?
L25      142347 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMO? OR ANTICARCINO? OR
                ANTINEOPLAS?
L26       22073 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIFUNG?
L28          27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND (L22 OR L23 OR L24 OR
                L25 OR L26)
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=> s (l21 or l27 or l28) not l5
          171 HAHM K?/AU
         9493 LEE D?/AU
         6802 PARK Y?/AU
        18572 KIM H?/AU
L56       28 (L21 OR L27 OR L28) NOT L5
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(authors - previously displayed)

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=> file medline; d que l33
FILE 'MEDLINE' ENTERED AT 15:55:55 ON 10 JUN 2003

 FILE LAST UPDATED: 8 JUN 2003 (20030608/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L31        159 SEA FILE=MEDLINE ABB=ON  PLU=ON  MAGAININ 2/CN
L32        119 SEA FILE=MEDLINE ABB=ON  PLU=ON  CECROPIN A/CN
L33          9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L31 AND L32

=> s l33 not l30
L57          9 L33 NOT L30
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(L30 = inventors, previously displayed)

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=> file embase; d que l39; d que l49
FILE 'EMBASE' ENTERED AT 15:56:32 ON 10 JUN 2003
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 FILE COVERS 1974 TO 5 Jun 2003 (20030605/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L35         26 SEA FILE=EMBASE ABB=ON  PLU=ON  MAGAININ 2 AND CECROPIN A
L36      12707 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIFUNGAL AGENT/CT
L37      21434 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIINFECTIVE AGENT/CT
L38      48668 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENT/CT
L39          7 SEA FILE=EMBASE ABB=ON  PLU=ON  L35 AND (L36 OR L37 OR L38)


L35         26 SEA FILE=EMBASE ABB=ON  PLU=ON  MAGAININ 2 AND CECROPIN A
L41         21 SEA FILE=EMBASE ABB=ON  PLU=ON  (ANTIBIOTIC OR ANTIMICROBIAL
               OR ANTINEOPLASTIC) AND L35
L43        140 SEA FILE=EMBASE ABB=ON  PLU=ON  MAGAININ 2/CT
L44         86 SEA FILE=EMBASE ABB=ON  PLU=ON  CECROPIN A/CT
L45         74 SEA FILE=EMBASE ABB=ON  PLU=ON  L43/MAJ
L46         50 SEA FILE=EMBASE ABB=ON  PLU=ON  L44/MAJ
L47          6 SEA FILE=EMBASE ABB=ON  PLU=ON  (L45 AND L44) OR (L46 AND L43)
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L48          6 SEA FILE=EMBASE ABB=ON  PLU=ON  L41 AND (L45 OR L46)
L49          7 SEA FILE=EMBASE ABB=ON  PLU=ON  L47 OR L48


=> s (139 or 149) not 134
L58         13 (L39 OR L49) NOT L34 (L34 = inventors, previously displayed)

=> file wpix; d que 153; d que 154
FILE 'WPIX' ENTERED AT 15:57:12 ON 10 JUN 2003
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FILE LAST UPDATED:          9 JUN 2003      <20030609/UP>
MOST RECENT DERWENT UPDATE:     200336        <200336/DW>
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L51          5 SEA FILE=WPIX ABB=ON  PLU=ON  MAGAININ 2
L52         77 SEA FILE=WPIX ABB=ON  PLU=ON  CECROPIN A
L53          3 SEA FILE=WPIX ABB=ON  PLU=ON  L51 AND L52


L54          0 SEA FILE=WPIX ABB=ON  PLU=ON  CA MA PEPTIDE


=> s l53 not l50
L59          3 L53 NOT L50 (L59 = inventors, previously displayed)

=> dup rem l57 l56 l58 l59
FILE 'MEDLINE' ENTERED AT 15:57:52 ON 10 JUN 2003

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PROCESSING COMPLETED FOR L57
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PROCESSING COMPLETED FOR L56
PROCESSING COMPLETED FOR L58
PROCESSING COMPLETED FOR L59
L60 39 DUP REM L57 L56 L58 L59 (14 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE MEDLINE
ANSWERS '10-30' FROM FILE HCAPLUS
ANSWERS '31-36' FROM FILE EMBASE
ANSWERS '37-39' FROM FILE WPIX

=> d ibib ab l60 1-39

L60 ANSWER 1 OF 39 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001013086 MEDLINE
DOCUMENT NUMBER: 20464935 PubMed ID: 11009597
TITLE: Role of the hinge region and the tryptophan residue in the synthetic antimicrobial peptides, cecropin A(1-8)-magainin 2(1-12) and its analogues, on their antibiotic activities and structures.
AUTHOR: Oh D; Shin S Y; Lee S; Kang J H; Kim S D; Ryu P D; Hahm K S; Kim Y
CORPORATE SOURCE: Department of Chemistry, Konkuk University, Seoul 143-701, Korea.
SOURCE: BIOCHEMISTRY, (2000 Oct 3) 39 (39) 11855-64.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1F0D; PDB-1F0E; PDB-1F0F; PDB-1F0G; PDB-1F0H
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001027

AB A 20-residue hybrid peptide CA(1-8)-MA(1-12) (CA-MA), incorporating residues 1-8 of cecropin A (CA) and residues 1-12 of magainin 2 (MA), has potent antimicrobial activity without toxicity against human erythrocytes. To investigate the effects of the Gly-Ile-Gly hinge sequence of CA-MA on the antibacterial and antitumor activities, two analogues in which the Gly-Ile-Gly sequence of CA-MA is either deleted (P1) or substituted with Pro (P2) were synthesized. The role of the tryptophan residue at position 2 of CA-MA on its antibiotic activity was also investigated using two analogues, in which the Trp2 residue of CA-MA is replaced with either Ala (P3) or Leu (P4). The tertiary structures of CA-MA, P2, and P4 in DPC micelles, as determined by NMR spectroscopy, have a short amphiphilic helix in the N-terminus and about three turns of alpha-helix in the C-terminus, with the flexible hinge region between them. The P1 analogue has an alpha-helix from Leu4 to Ala14 without any hinge structure. P1 has significantly decreased lytic activities against bacterial and tumor cells and PC/PS vesicles (3:1, w/w), and reduced pore-forming activity on lipid bilayers, while P2 retained effective lytic activities and pore-forming activity. The N-terminal region of P3 has a flexible structure without any specific secondary structure. The P3 modification caused a drastic decrease in the antibiotic activities, whereas P4, with the hydrophobic Leu side chain at position 2, retained its activities. On the basis of the tertiary structures, antibiotic activities, vesicle-disrupting activities, and pore-forming activities, the structure-function relationships can be summarized as follows. The partial insertion of the Trp2 of CA-MA into the membrane, as well as the electrostatic interactions between the positively charged Lys residues at the N-terminus of the CA-MA and the anionic phospholipid headgroups, leads to the primary binding to the cell membrane. Then, the flexibility or bending potential induced by

the Gly-Ile-Gly hinge sequence or the Pro residue in the central part of the peptides may allow the alpha-helix in the C-terminus to span the lipid bilayer. These structural features are crucial for the potent antibiotic activities of CA-MA.

L60 ANSWER 2 OF 39 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999209820 MEDLINE
DOCUMENT NUMBER: 99209820 PubMed ID: 10195445
TITLE: Structure-antibacterial, antitumor and hemolytic activity relationships of cecropin A-magainin 2 and cecropin A-melittin hybrid peptides.
AUTHOR: Shin S Y; Kang J H; Hahm K S
CORPORATE SOURCE: Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, KIST, Yusong, Taejon, Korea.
SOURCE: JOURNAL OF PEPTIDE RESEARCH, (1999 Jan) 53 (1) 82-90. Journal code: 9707067. ISSN: 1397-002X.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990610

AB In order to elucidate the structure-antibiotic activity relationship of cecropin A-magainin 2 and cecropin A-melittin hybrid peptides, several truncated peptides and the analogues with amino acid substitutions were synthesized and their antibacterial, antitumor and hemolytic activities of were examined. Cecropin A-magainin 2 hybrid analog, L16-CA(1-8)-MA(1-12) (termed as L-CA-MA in this study: KWKLFKKIGIGKFLHLAKKF-NH2), is known to have potent antibacterial and antitumor activity with less hemolytic activity. We found that the C-terminal region of L-CA-MA is more involved in the alpha-helical structure on cell membrane-like environment than N-terminal one by circular dichroism analysis. Deletion of the Gly-Ile-Gly sequence, the central hinge region of L-CA-MA, produced a considerable reduction in antitumor and hemolytic activity rather than an antibacterial one. The insertion of Pro, Gly-Ile or Gly-Pro in this hinge region of L-CA-MA caused retention of both antibacterial and antitumor activity while causing a significant decrease in hemolytic activity. However, the substitution with Gly-Pro-Gly instead of the Gly-Ile-Gly in CA(1-8)-MA(1-12), CA(1-8)-ME(1-12), CA(1-13)-MA(1-13) and CA(1-13)-ME(1-13) hybrids resulted in a drastic decrease in antibacterial, antitumor and hemolytic activity. The increase of hydrophobicity at position 16 in CA(1-8)-MA(1-12) by substituting Trp or Phe induced a significant increase in hemolytic activity without a considerable change in either antibacterial or antitumor activity. Therefore, these results suggested that the appropriate flexibility in the hinge region of CA-MA and CA-ME hybrid peptides and the appropriate hydrophobicity at position 16 in the hydrophobic region of CA (1-8)-MA(1-12) are important in potent antibacterial and antitumor activity with no hemolytic effect.

L60 ANSWER 3 OF 39 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998285223 MEDLINE
DOCUMENT NUMBER: 98285223 PubMed ID: 9623765
TITLE: Cecropin A - magainin 2 hybrid peptides having potent antimicrobial activity with low hemolytic effect.
AUTHOR: Shin S Y; Kang J H; Lee M K; Kim S Y; Kim Y; Hahm K S
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, KIST, Yusong, Taejon.
SOURCE: BIOCHEMISTRY AND MOLECULAR BIOLOGY INTERNATIONAL, (1998 May) 44 (6) 1119-26.

Journal code: 9306673. ISSN: 1039-9712.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980820
Last Updated on STN: 19980820
Entered Medline: 19980812

AB In order to obtain peptides having improved antimicrobial activity with low hemolytic effect, a hybrid peptide (CA-MA) composed from cecropin A (1-8) and magainin 2(1-12), and its analogues with amino acid substitutions were designed and synthesized. The antimicrobial activities against bacterial cells and hemolytic activities against human red blood cells were analyzed for each peptide. Secondary structures of the peptides in aqueous solution, 50% trifluoroethanol, and sodium dodecylsulfate micelles were estimated using circular dichroism spectroscopy. The increase in hydrophobicity or alpha-helicity of the peptides correlated with an increase in hemolytic activity rather than antimicrobial activity. The substitution of Leu for Ser at position 16 in CA-MA resulted in a remarkable increase in antimicrobial activity without a significant change in hemolytic activity. Furthermore, the increase in antimicrobial activity of the peptides was not always accompanied by the increase in hemolytic activity.

L60 ANSWER 4 OF 39 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998380107 MEDLINE
DOCUMENT NUMBER: 98380107 PubMed ID: 9716250
TITLE: Release of aqueous contents from phospholipid vesicles induced by cecropin A (1-8)-magainin 2 (1-12) hybrid and its analogues.
AUTHOR: Kang J H; Shin S Y; Jang S Y; Lee M K; Hahm K S
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea, Research Institute of Bioscience and Biotechnology, Yusong, Taejon.
SOURCE: JOURNAL OF PEPTIDE RESEARCH, (1998 Jul) 52 (1) 45-50.
Journal code: 9707067. ISSN: 1397-002X.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981028

AB The membrane-disrupting properties of cecropin A (1-8)-magainin 2 (1-12) hybrid peptide, which has higher antitumor with less hemolytic activities than cecropin A (1-8)-melittin (1-12), and its analogues were assessed by measuring the induced release of vesicle-entrapped fluorescence probes. A model membrane was made of zwitterionic phospholipid (phosphatidylcholine) or the mixture of negatively and zwitterionic phospholipids (phosphatidylcholine and phosphatidylserine). The extent of leakage of the aqueous content of the phospholipid vesicles was found to have remarkable discrepancies according to the amphipathic nature of each analogue peptide. The entrapped high molecular weight solute (fluorescein-labeled immunoglobulin G, 55 kDa) also was released by the analogue which had the largest hydrophobic region and the highest amphipathic score among peptides tested. As the result of the determination of the relationships between the membrane-disrupting properties and the hydrophobicity values of peptides, it was found that the membrane-disrupting activity increased according to increasing the hydrophobicity of the peptide. The tryptophan fluorescence emission

spectra and CD spectra showed that on interaction with the phospholipid vesicle, the peptide acquired the ordered structure and alpha-helical conformation by moving a tryptophan residue into the nonpolar environment of the phospholipid vesicle. These results suggest that the breakdown of the lipid bilayer was mediated by the alpha-helical amphipathic structure of the peptide interacting with the lipid bilayers as well as the by the hydrophobicity of the peptide.

L60 ANSWER 5 OF 39 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998013743 MEDLINE
DOCUMENT NUMBER: 98013743 PubMed ID: 9352466
TITLE: Structure-antitumor and hemolytic activity relationships of synthetic peptides derived from cecropin A-magainin 2 and cecropin A-melittin hybrid peptides.
AUTHOR: Shin S Y; Lee M K; Kim K L; Hahm K S
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, KIST, Taejon, Korea.
SOURCE: JOURNAL OF PEPTIDE RESEARCH, (1997 Oct) 50 (4) 279-85. Journal code: 9707067. ISSN: 1397-002X.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971222

AB The hybrid peptide (CA-ME) derived from cecropin A(1-8) and melittin (1-12) has potent antibacterial and antimalarial activities. Because the N-terminal sequence 1-12 of magainin 2 is similar to melittin(1-12), CA-MA with CA(1-8) and MA(1-12) and their analogues were designed and synthesized. Antitumor activities of these peptides were evaluated using three small cell lung cancer cell lines. Greater antitumor activity was observed when the residues 16, 18 and 19 of the peptide were hydrophobic (Leu or Val), basic (Lys) and basic (Lys), respectively. The IC50 values of the peptides with the residues were 2 to 4 microM. Residue 12 was related to hemolytic activity rather than antitumor activity. Increase in amphipathicity of P4 enhanced hemolytic activity without significant change in antitumor activity. The alpha-helicity of the peptides in a 30 mM sodium dodecyl sulfate solution was more closely correlated to hemolytic activity than antitumor activity.

L60 ANSWER 6 OF 39 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 94333367 MEDLINE
DOCUMENT NUMBER: 94333367 PubMed ID: 8055943
TITLE: Antibacterial peptides and mitochondrial presequences affect mitochondrial coupling, respiration and protein import.
AUTHOR: Hugosson M; Andreu D; Boman H G; Glaser E
CORPORATE SOURCE: Department of Biochemistry, Arrhenius Laboratories for Natural Sciences, Stockholm University, Sweden.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Aug 1) 223 (3) 1027-33. Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940920
Last Updated on STN: 19940920

Entered Medline: 19940915

AB Cecropins A and P1, antibacterial peptides from insects and from pig and some related peptides released respiratory control, inhibited protein import and at higher concentrations also inhibited respiration. However, PR-39, an antibacterial peptide from pig intestine, was found to be almost inert towards mitochondria. The concentrations at which the three mitochondrial functions were effected varied for different peptides. Melittin, magainin and Cecropin-A-(1,13)-Melittin(1,13)-NH2, a hybrid between cecropin A and melittin, were most potent, while the two cecropins acted at higher concentrations. The biosynthesis of cecropin A is known and the intermediates are synthesized. We have used four peptides from this pathway to investigate their effects on coupling, respiration and protein import into mitochondria. Mature cecropin A followed by the preproprotein were most aggressive whereas the intermediates were less active or inert. The efficiency of different derivatives of cecropin A as uncouplers correlates well with their capacity to release membrane potential measured as fluorescence quenching of Rhodamine 123. Inhibition of respiration was found to be dependent on membrane potential and was most pronounced with mature cecropin A, less so with its three precursors. We also found that three peptides derived from mitochondrial presequences showed antibacterial activity. It is concluded that, there are similarities in the functions of antibacterial peptides and mitochondrial presequences, uncoupling activity in mitochondria cannot be correlated with the antibacterial activity (contrary to a previous suggestion), the processing of preprocecropin A may have evolved in such a way that there is a minimum of membrane damage from the intermediates in the pathway, and peptides produced for delivery outside of an animal have evolved to be more aggressive against mitochondria than peptides for delivery inside of the animal.

L60 ANSWER 7 OF 39 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 90280455 MEDLINE
DOCUMENT NUMBER: 90280455 PubMed ID: 1693777
TITLE: All-D amino acid-containing channel-forming antibiotic peptides.
AUTHOR: Wade D; Boman A; Wahlin B; Drain C M; Andreu D; Boman H G; Merrifield R B
CORPORATE SOURCE: Rockefeller University, New York, NY 10021.
CONTRACT NUMBER: DK 01260 (NIDDK)
GM 25693 (NIGMS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Jun) 87 (12) 4761-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900824
Last Updated on STN: 19970203
Entered Medline: 19900719

AB The D enantiomers of three naturally occurring antibiotics--cecropin A, magainin 2 amide, and melittin--were synthesized. In addition, the D enantiomers of two synthetic chimeric cecropin-melittin hybrid peptides were prepared. Each D isomer was shown by circular dichroism to be a mirror image of the corresponding L isomer in several solvent mixtures. In 20% hexafluoro-2-propanol the peptides contained 43-75% alpha-helix. The all-D peptides were resistant to enzymatic degradation. The peptides produced single-channel conductances in planar lipid bilayers, and the D and L enantiomers caused equivalent amounts of electrical conductivity. All of the peptides were potent antibacterial agents against

representative Gram-negative and Gram-positive species. The D and L enantiomers of each peptide pair were equally active, within experimental error. Sheep erythrocytes were lysed by both D- and L-melittin but not by either isomer of cecropin A, magainin 2 amide, or the hybrids cecropin A-(1-13)-melittin-(1-13)-NH2 or cecropin A-(1-8)-melittin-(1-18)-NH2. The infectivity of the bloodstream form of the malaria parasite Plasmodium falciparum was also inhibited by the D and L hybrids. It is suggested that the mode of action of these peptides on the membranes of bacteria, erythrocytes, plasmodia, and artificial lipid bilayers may be similar and involves the formation of ion-channel pores spanning the membranes, but without specific interaction with chiral receptors or enzymes.

L60 ANSWER 8 OF 39 MEDLINE
ACCESSION NUMBER: 97252706 MEDLINE
DOCUMENT NUMBER: 97252706 PubMed ID: 9096062
TITLE: Structure and functions of channel-forming peptides: magainins, cecropins, melittin and alamethicin.
AUTHOR: Bechinger B
CORPORATE SOURCE: Max-Planck-Institut fur Biochemie, Am Klopferspitz 18a, 82152 Martinsried, Germany.
SOURCE: JOURNAL OF MEMBRANE BIOLOGY, (1997 Apr 1) 156 (3) 197-211. Ref: 262
Journal code: 0211301. ISSN: 0022-2631.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970612

L60 ANSWER 9 OF 39 MEDLINE
ACCESSION NUMBER: 96425793 MEDLINE
DOCUMENT NUMBER: 96425793 PubMed ID: 8828135
TITLE: The effects of magainin 2, cecropin, mastoparan and melittin on Brucella abortus.
AUTHOR: Halling S M
CORPORATE SOURCE: USDA/ARS/NADC, Ames, IA 50010 USA.. shalling@asrr.arsusda.gov
SOURCE: VETERINARY MICROBIOLOGY, (1996 Jul) 51 (1-2) 187-92.
Journal code: 7705469. ISSN: 0378-1135.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961203

AB The effect of the alpha-helical polycationic peptides magainin 2, melittin, mastoparan and cecropin on the viability of Brucella abortus 544 (type species), B. abortus S19 (vaccine strain) and B. abortus S2308 (vaccine challenge strain) was determined. Rough mutants of these strains and the rough candidate vaccine strain B. abortus RB51 were also tested. S. typhimurium was used as a control. The peptides did not affect the viability of B. abortus smooth strains but some of the peptides affected viability of the rough strains. Magainin 2 at a concentration of 100 micrograms ml-1 did not reduce the viability of the rough B. abortus

strains. Cecropin at a concentration of 15 micrograms ml-1 reduced the viability of the rough strains by approximately 10-fold. Mastoparan at a concentration of 50 micrograms ml-1 reduced the viability of the rough strains by approximately 100-fold. Melittin at a concentration of 20 micrograms ml-1 reduced the viability of the rough strains of B. abortus by approximately 1000-fold. The brucellae were significantly more resistant to all the cationic peptides than was S. typhimurium.

L60 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:256728 HCAPLUS
DOCUMENT NUMBER: 133:28393
TITLE: Design of novel antimicrobial peptides based on structure-antibiotic activity relationships of **cecropin A, magainin** 2 and melittin
AUTHOR(S): Shin, Song Yub; Kang, Joo Hyun; Lee, Dong Gun; Hahm, Kyung-Soo
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-600, S. Korea
SOURCE: Journal of Biochemistry, Molecular Biology and Biophysics (2000), 4(2), 135-145
CODEN: JBMBF6; ISSN: 1025-8140
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of **cecropin A** (CA)-**magainin** 2 (MA) and **cecropin A** (CA)-melittin (ME) with amino acid substitutions were designed and synthesized in order to investigate structure-antibiotic activity relationships of these hybrid peptides. An increase in hydrophobicity or .alpha.-helicity of the peptides was correlated with an increase in hemolytic activity rather than antimicrobial activity. Membrane disrupting properties of CA-MA hybrids, measured by the induced release of vesicle-entrapped calcein, were found to have remarkable discrepancies according to the amphipathic nature of each peptide. Tryptophan fluorescence spectra showed that upon interaction with the phospholipid vesicle, the peptide acquired an ordered structure and .alpha.-helical conformation by moving a tryptophan residue into the nonpolar environment of the phospholipid vesicle. **Antifungal** peptide (K18,19-CA-ME) was shown by using fluorescence activated flow cytometric anal. and confocal laser scanning microscopy, to act by forming pores or ion channels on cell membranes of T. beigelii .
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 1997:259025 HCAPLUS
DOCUMENT NUMBER: 126:261441
TITLE: **Antifungal** activities of **magainin** -2 hybrid peptides against Trichosporon beigelii
AUTHOR(S): Lee; Gun, Dong; Shin, Song Yub; Lee, Sung Gu; Kim, Kil Lyong; Lee, Myung Kyu; Hahm, Kyung Soo
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, KIST, Taejon, 305-600, S. Korea
SOURCE: Journal of Microbiology and Biotechnology (1997), 7(1), 49-51
CODEN: JOMBES; ISSN: 1017-7825
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to obtain a synthetic peptide with a more potent **antifungal** activity than **magainin**-2 but without hemolytic activity, four hybrid peptides were designed from the sequences of **magainin** 2 and **cecropin A** and their **antifungal** activities against Trichosporon beigelii were investigated. The result showed that analog 2 and 4 exhibited better **antifungal** activity against T. beigelii than **magainin**-2 but no hemolytic activities. The peptides, therefore, could be used as models for the development of potent **antifungal** peptides.

L60 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:23366 HCAPLUS
DOCUMENT NUMBER: 138:78538
TITLE: Biomedical devices with antimicrobial cationic peptide and protein coatings
INVENTOR(S): Wilcox, Mark; Vanderlaan, Doug; Aliwarga, Yulina; Lun, Jenny
PATENT ASSIGNEE(S): Australia
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003007993	A1	20030109	US 2000-516636	20000301

PRIORITY APPLN. INFO.: US 2000-516636 20000301

AB Biomedical devices, such as contact lenses, with antimicrobial coatings are provided. One or more surfaces of the device are coated with a cationic peptide, cationic proteins, or mixts. thereof to impart antimicrobial properties to the surface. For example, Etafilcon A lenses were incubated in concns. of cationic proteins/peptides, after rinsing bacteria were added, and nos. of cells analyzed. Although nisin and **cecropin A** did not reduce the total adhesion of bacteria by increasing the total no. of cells on the lens, there was a significant redn. in the viability of those cells compared to the cells adhered to the uncoated lens. This indicates that the adhered bacteria were prevented from growing. Protamine significantly reduced the adhesion of Pseudomonas aeruginosa 6294 to the lenses and also reduced the viability of the cells on the coated lenses. Melittin both reduced initial adhesion of Staphylococcus aureus 31. A similar effect was seen for P. aeruginosa 6294 and when a mixt. of protamine and melittin was used.

L60 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:717050 HCAPLUS
DOCUMENT NUMBER: 137:232921
TITLE: Design, preparation, and properties of **antibacterial** .beta.-peptides
INVENTOR(S): Degrado, William F.; Hamuro, Yoshimoto; Liu, Dahui
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2002132766 A1 20020919 US 2000-732911 20001211
PRIORITY APPLN. INFO.: US 2000-732911 20001211
OTHER SOURCE(S): MARPAT 137:232921
AB **Antibacterial** .beta.-peptides I [R1, R3 = H, alkyl, Ph, heteroaryl, alkylaryl; R2 = (CH2)mNH2 (m = 1-5), (CH2)xNHC:NHNH2 (x = 1-5), pyridyl, alkylpryidyl, amidine-substituted benzyl, Ph, or a cyclic amidine group; X = NH2, OH, NHR, or OR, where R = alkylaryl or acyl group, either free or polymer-supported, (un)substituted carboxamide, or a polymer; Y = H, alkyl, acyl, acyl-terminated polymer, a sulfonamide, an ether, a urea, a urethane, or a polymer; n = 2-7] are claimed. Thus, .beta.-peptides H-(h-Ala-h-Lys-h-Val)n-OH (n = 4 or 5) were prepd. by the solid-phase method and were shown to adopt an L+2 helix conformation upon binding to lipid micelle or vesicle. They have high **antibacterial** activity against bacteria with IC50 of several .mu.Ms and low toxicity towards mammalian cells.

L60 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:924439 HCAPLUS
DOCUMENT NUMBER: 136:193718
TITLE: Correlation of the **antibacterial** activities of cationic peptide antibiotics and cationic steroid antibiotics
AUTHOR(S): Ding, Bangwei; Guan, Qunying; Walsh, Joshua P.; Boswell, J. Scott; Winter, Tim W.; Winter, Erica S.; Boyd, Stephanie S.; Li, Chunhong; Savage, Paul B.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(3), 663-669
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **antibacterial** activities of cationic steroid antibiotics and cationic peptide antibiotics have been compared. Depolarization of bacterial membranes, activation of bacterial stress-related gene promoters, and changes in bacterial morphologies caused by these antibiotics suggest that cationic steroid and peptide antibiotics share mechanistic aspects. Modified cationic steroid antibiotics display improved selectivity for prokaryotic cells over eukaryotic cells presumably due to increased charge recognition.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:30950 HCAPLUS
DOCUMENT NUMBER: 132:219403
TITLE: Cationic peptide antimicrobials induce selective transcription of micF and osmY in Escherichia coli
AUTHOR(S): Oh, J.-T.; Cajal, Y.; Skowronska, E. M.; Belkin, S.; Chen, J.; Van Dyk, T. K.; Sasser, M.; Jain, M. K.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Delaware, Newark, DE, USA
SOURCE: Biochimica et Biophysica Acta (2000), 1463(1), 43-54
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cationic antimicrobial peptides, such as polymyxin and cecropin, activated transcription of osmY and micF in growing Escherichia coli independently of each other. The micF response required the presence of a functional rob gene. It is intriguing that in this and other assays an identical

response profile was also seen with hyperosmotic salt or sucrose gradient, two of the most commonly used traditional food preservatives. The osmY and micF transcription was not induced by hypoosmotic gradient, ionophoric peptides, uncouplers, or with other classes of membrane perturbing agents. The **antibacterial** peptides did not promote transcription of genes that respond to macromol. or oxidative damage, fatty acid biosynthesis, heat shock, or depletion of proton or ion gradients. These and other results show that the **antibacterial** cationic peptides induce stasis in the early growth phase, and the transcriptional efficacy of **antibacterial** peptides correlates with their min. inhibitory concn., and also with their ability to mediate direct exchange of phospholipids between vesicles. The significance of these results is developed as the hypothesis that the cationic peptide antimicrobials stress growth of Gram-neg. organisms by making contacts between the two phospholipid interfaces in the periplasmic space and prevent the hyperosmotic wrinkling of the cytoplasmic membrane. Broader significance of these results, and of the hypothesis that the peptide mediated contacts between the periplasmic phospholipid interfaces are the primary triggers, is discussed in relation to **antibacterial** resistance.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:577056 HCAPLUS
DOCUMENT NUMBER: 131:209109
TITLE: Methods for identifying polycationic, peptide-like compounds with **antibacterial** activity
INVENTOR(S): Van Dyk, Tina K.; Cajal, Yolanda; Jain, Mehendra Kumar
PATENT ASSIGNEE(S): E.I. du Pont de Nemours and Co., USA; University of Delaware
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945152	A1	19990910	WO 1999-US4795	19990305
W: AU, CA, IL, JP, KR, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2321931	AA	19990910	CA 1999-2321931	19990305
AU 9928950	A1	19990920	AU 1999-28950	19990305
EP 1060268	A2	20001220	EP 1999-909832	19990305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002505120	T2	20020219	JP 2000-534683	19990305

PRIORITY APPLN. INFO.: US 1998-77025P P 19980306
US 1998-100257P P 19980914
WO 1999-US4795 W 19990305

AB A method is provided for identifying polycationic, peptide-like compds. characterized by **antibacterial** activity against gram neg. bacteria. The method takes advantage of the induction of hyperosmotic stress without leakage of cytoplasmic content. The method involves detg. whether the compd. has the ability to produce phospholipid exchange between the lipid bilayers in conjunction with the induction of the osmotic stress response in the target cell. Detg. the induction of the osmotic stress response is effected using a bioluminescent detector organism having a osmY-LUX gene fusion.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:251850 HCAPLUS
DOCUMENT NUMBER: 131:71111
TITLE: Modulation of **antibacterial** peptide activity by products of Porphyromonas gingivalis and Prevotella spp.
AUTHOR(S): Devine, D. A.; Marsh, P. D.; Percival, R. S.; Rangarajan, M.; Curtis, M. A.
CORPORATE SOURCE: Leeds Dental Institute, University of Leeds, Leeds, LS2 9LU, UK
SOURCE: Microbiology (Reading, United Kingdom) (1999), 145(4), 965-971
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated the ability of anaerobic periodontal bacteria to inactivate and resist killing by antimicrobial peptides through prodn. of extracellular proteases. **Antibacterial** activities of peptides were assessed in a double-layer agarose diffusion assay, and MICs and MBCs were detd. in broth microdilution assays. Culture supernates of Porphyromonas gingivalis and Prevotella spp. inactivated mastoparan, **magainin** II and cecropin B while Gram-pos. oral supragingival bacteria had no effect. Inactivation was prevented by protease inhibitors and was unaffected by 45% human serum. Purified proteases from the periodontopathogen Porph. gingivalis inactivated peptides [cecropin B, brevinin, CAMEL (**cecropin A** 1-7 + melittin 2-9), mastoparan] as would be predicted from the amino acid sequences of the peptides and the known bond specificities of these Arg-x and Lys-x enzymes. MALDI-TOF MS revealed that inactivation of cecropin B by Porph. gingivalis protease was due to specific cleavage of the mol. Inactivation of cecropin B by proteases took 10-15 min. Paradoxically, MICs of cecropin B against Porph. gingivalis and Prevotella intermedia were low, while Prevotella nigrescens was resistant, suggesting that prodn. of proteases alone is insufficient to protect Porph. gingivalis and Prev. intermedia from the action of antimicrobial peptides. Thus, antimicrobial peptides could be developed as therapeutic agents targeted against specific periodontal pathogens.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:578727 HCAPLUS
DOCUMENT NUMBER: 132:122896
TITLE: Structure-biological activity relationships of **cecropin A** (1-8)-**magainin** 2 (1-12) hybrid and its analogues
AUTHOR(S): Shin, S. Y.; Kang, J. H.; Lee, D. G.; Kim, S. Y.; Lee, M. K.; Hahm, K.-S.
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-600, S. Korea
SOURCE: Peptide Science: Present and Future, Proceedings of the International Peptide Symposium, 1st, Kyoto, Nov. 30-Dec. 5, 1997 (1999), Meeting Date 1997, 269-270. Editor(s): Shimonishi, Yasutsugu. Kluwer: Dordrecht, Neth.
CODEN: 68BYA5
DOCUMENT TYPE: Conference

LANGUAGE: English
AB A symposium discussing the authors' prepn. and evaluation of **cecropin A**(1-8)-**magainin** 2(1-12) hybrid peptides for hemolytic, **antibacterial**, and anti-tumor activity, and its relationship to peptide .alpha.-helicity.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:275209 HCAPLUS
DOCUMENT NUMBER: 131:71113
TITLE: Influence on the cell membrane of Trichosporon beigelii by fungicidal peptide derived from **cecropin A**(1-8)-**magainin** 2(1-12)
AUTHOR(S): Lee, Dong Gun; Maeng, Cheol-Young; Shin, Song Yub; Hahm, Kyung-Soo
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-600, S. Korea
SOURCE: Journal of Biochemistry, Molecular Biology and Biophysics (1999), 2(4), 243-248
CODEN: JBMBF6; ISSN: 1025-8140
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fungicidal activities of the **cecropin A**(1-8)-**magainin** 2(1-12) (CA-MA) and its analogs with amino acid substitution were measured by a growth inhibition assay using Trichosporon beigelii. CA-MA displayed potent fungicidal activity (minimal inhibitory concn.: 5 .mu.g/mL) against Trichosporon beigelii with no hemolytic activity. Substitution (A12-CA-MA: analog 2) of Ala to Lys at position 12 of CA-MA caused an increase in fungicidal activity without any increase in hemolytic activity. In order to investigate the fungicidal mechanism of analog 2, it was reacted with Trichosporon beigelii protoplasts. The morphol. changes and the failure of the cell wall regeneration of the protoplast by analog 2 were obsd. Moreover, the amts. of released potassium ion by the peptide were increased. These results suggested that the fungicidal mechanism of analog 2 may be due to the pore formation or the detergent-like disruption of cell membranes.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:621235 HCAPLUS
DOCUMENT NUMBER: 129:254975
TITLE: Compositions and methods for treating infections using cationic peptides alone or in combination with antibiotics
INVENTOR(S): Fraser, Janet R.; West, Michael H. P.; Mcnicol, Patricia J.
PATENT ASSIGNEE(S): Micrologix Biotech Inc., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9840401	A2	19980917	WO 1998-CA190	19980310
WO 9840401	A3	19981217		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6180604	B1	20010130	US 1997-915314	19970820
AU 9866047	A1	19980929	AU 1998-66047	19980310
EP 966481	A2	19991229	EP 1998-907779	19980310

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002544759	T2	20021224	JP 1998-538997	19980310

PRIORITY APPLN. INFO.:

US 1997-40649P	P	19970310
US 1997-915314	A	19970820
US 1997-60099P	P	19970926
US 1996-24754P	P	19960821
US 1997-34949P	P	19970113
US 1998-30619	A	19980225
WO 1998-CA190	W	19980310

AB Compns. and methods for treating infections, esp. bacterial infections, are provided. Cationic peptides in combination with an antibiotic agent are administered to a patient to enhance the activity of the antibiotic agent, overcome tolerance, and overcome acquired or inherent resistance. Thus, a combination of antimicrobial agent and cationic peptide that breaks tolerance results in a decrease of min. bacterial concn. (MBC) to min. inhibitory concn. (MIC) ratio to <32. The combination of vancomycin and MBI 26 overcomes the tolerance of Enterococcus casseliflavus and E. faecalis with MBC/MIC ratio of 1-8 compared to that of 32 to >256 for vancomycin alone.

L60 ANSWER 21 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:115396 HCAPLUS
DOCUMENT NUMBER: 128:176152
TITLE: **Antibacterial** and antimalarial hybrid peptides
INVENTOR(S): Boman, Hans G.; Merrifield, Robert B.; Andreu, David
PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 831,462, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5714467	A	19980203	US 1993-39557	19930326

PRIORITY APPLN. INFO.:

US 1989-336777	19890412
US 1989-449593	19891212
US 1992-831462	19920205

AB The invention relates to **antibacterial** and antimalarial peptides which are hybrid peptides which are derived from naturally occurring peptides such as cecropins, attacins, **magainins**, sarcotoxin, sapecin, bactenecins, alamethidicins, defensins and PGLa, and toxins such as streptolysins, melittin, barbatolysin, paradaxins and delta hemolysin. The hybrid peptides of the present invention are easily synthesized and

have reduced toxicity. Also included in the invention are pharmaceutical compns. contg. such hybrid peptides, and methods of treating patients infected with an organism against which these peptides are active.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:222499 HCAPLUS
DOCUMENT NUMBER: 126:222741
TITLE: Effect of natural amphipathic peptides on viability, membrane potential, cell shape and motility of mollicutes
AUTHOR(S): Beven, L.; Wroblewski, H.
CORPORATE SOURCE: Groupe "Membrances et Osmoregulation", UPRES-A CNRS Q6026 et CNRS GDR n.degree. 1153, Universite de Rennes 1, Rennes, 35042, Fr.
SOURCE: Research in Microbiology (1997), 148(2), 163-175
CODEN: RMCREW; ISSN: 0923-2508
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antibiotic activity of ten amphipathic peptides was investigated in six species of mollicutes belonging to the genera Acholeplasma, Mycoplasma and Spiroplasma. A. laidlawii was the most sensitive and M. mycoides subsp. mycoides SC the most resistant. Animal defense peptides (**cecropins A** and P1 and **magainin** 2) proved to be less potent than bee-venom mellitin and most of the peptides produced by bacteria (globomycin, gramicidin S, surfactin and valinomycin) or fungi (alamethicin). Gramicidin S was by far the most active peptide, with minimal inhibitory concns. ranging from 2 to 50 nM. Alamethicin, gramicidin S, mellitin and surfactin had a cidal effect, while cecropins, globomycin, **magainin** 2, polymyxin B and valinomycin proved to be static. The peptides altered the membrane potential of spiroplasma cells with a potency independent of their linear or cyclic structure. However, globomycin depolarized the plasma membrane only weakly, while polymyxin B, in order to be active, required prior hyperpolarization of the membrane. The peptides also induced the loss of cell motility and helicity in spiroplasmas, suggesting that motility and cell shape in these bacteria are coupled to the transmembrane electrochem. gradient. Globomycin, an inhibitor of signal-peptidase II, prevented the growth of spiroplasmas, M. gallisepticum, and M. genitalium, but not that of A. laidlawii and M. mycoides subsp. mycoides SC, although the latter also synthesized membrane lipoproteins. Inhibition of spiralin processing by globomycin was demonstrated in S. citri and S. melliferum, with a more pronounced effect in the second species.

L60 ANSWER 23 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:49226 HCAPLUS
DOCUMENT NUMBER: 126:155047
TITLE: Antibiotic peptides containing D-amino acids
INVENTOR(S): Merrifield, Robert B.; Wade, David; Boman, Hans G.
PATENT ASSIGNEE(S): The Rockefeller University, USA
SOURCE: U.S., 8 pp., Cont. of U.S. Ser. No. 87,143, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5585353 A 19961217 US 1994-307479 19940916
PRIORITY APPLN. INFO.: US 1990-474524 19900202
US 1993-87143 19930706

AB Antibiotically and/or antimalarially active enantiomers of naturally occurring antibiotics such as **cecropins A**, B, and D, melittin, **magainins** I and II, and their addn., deletion, and replacement analogs, including homologous and heterologous analogs thereof, synthesized from D-amino acids by solid-phase peptide synthesis are claimed.

L60 ANSWER 24 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:19676 HCAPLUS
DOCUMENT NUMBER: 126:129147
TITLE: **Antibacterial** activities of peptides designed as hybrids of antimicrobial peptides
AUTHOR(S): Shin, Song Yub; Kang, Joo Hyun; Lee, Myung Kyu; Hahm, Kyung-Soo
CORPORATE SOURCE: Peptide Eng. Research Unit, Korea Res. Inst. Bioscience Biotechnology, Taejon, 305-600, S. Korea
SOURCE: Journal of Biochemistry and Molecular Biology (1996), 29(6), 545-548
CODEN: JBMBE5; ISSN: 1225-8687
PUBLISHER: Biochemical Society of the Republic of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CA(1-8)ME(1-12), the CA-ME hybrid peptide of the amino terminal segments of **cecropin A** (CA) and melittin (ME), has been reported to have a broad spectrum and improved potency without a hemolytic property. In order to obtain new synthetic peptides with powerful **antibacterial** activity without hemolytic activity, several hybrid peptides were designed from the sequences of **cecropin A** (CA), honeybee melittin (ME), **magainin** 2, bombinin and lactoferricin. All hybrid peptides were constructed to form an amphipathically basic-flexible-hydrophobic structure and synthesized by the solid phase method. Their hemolytic activities against human red blood cells and **antibacterial** activities against both Gram-pos. and Gram-neg. bacteria were detd. CA(1-8)MA(1-12), CA(1-8)BO(1-12), MA(10-17)ME(1-12) and LF(20-29)ME(1-12) showed comparable activities with broad spectra against both Gram-pos. and Gram-neg. bacteria relative to CA(1-8)ME(1-12) but without hemolytic properties. These hybrid peptides, therefore, could be useful as model peptides to design a novel peptide with improved **antibacterial** activity and study on structure-activity relationships of antimicrobial peptides.

L60 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:83931 HCAPLUS
DOCUMENT NUMBER: 126:155012
TITLE: **Antifungal** effect of melittin-hybrid synthetic peptides for Fusarium oxysporum
AUTHOR(S): Lee, Dong-Gun; Shin, Song-Yub; Lee, Sung-Gu; Lee, Myung-Kyu; Hahm, Kyung-Soo
CORPORATE SOURCE: Peptide Engineering Research Unit, Korea Research Institute Bioscience and Biotechnology, Taejon, 305-600, S. Korea
SOURCE: Sanop Misaengmul Hakhoechi (1996), 24(5), 529-533
CODEN: SMHAEH; ISSN: 0257-2389
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB Melittin (ME) from honeybee venom has a broad range of strong antimicrobial activity, but it has hemolytic activity against eukaryotic

cells. In order to design peptides with powerful **antifungal** activity without cytotoxic property of ME and understand structure-**antifungal** activity relationships, hybrid peptides derived from the sequences of ME and **cecropin A** (CA) or **magainin** 2 (MA), MA(10-17)ME(1-12) and CA(1-8)ME(1-12), were synthesized by a solid phase method. MA(10-17)ME(1-12) showed potent **antifungal** activity comparable to ME against Fusarium oxysporum with no hemolytic activity against human red blood cells. The hybrid peptides showed strong inhibition of (1,3)-.beta.-.delta.-glucan synthase. This result indicates that the **antifungal** activity of the hybrid peptides against Fusarium oxysporum is attributed to the inhibition of cell wall synthesis. The results, therefore, depict a successful design of a peptide having **antifungal** activity without hemolytic property.

L60 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:718963 HCAPLUS
DOCUMENT NUMBER: 123:167535
TITLE: The outer membranes of Brucella spp. are resistant to **bactericidal** cationic peptides
AUTHOR(S): Martinez de Tejada, G.; Pizarro-Cerda, J.; Moreno, E.; Moriyon, I.
CORPORATE SOURCE: Dep. Microbiol., Univ. Navarra, Pamplona, Spain
SOURCE: Infection and Immunity (1995), 63(8), 3054-61
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The actions of polymyxin B, rabbit polymorphonuclear lysosome exts., 14 polycationic peptides (including defensin NP-2, cecropin P1, lactoferricin B, and active peptides from cationic protein 18 and bactenecin), EDTA, and Tris on Brucella spp. were studied, with other gram-neg. bacteria as controls. Brucella spp. were comparatively resistant to all of the agents listed above and bound less polymyxin B, and their outer membranes (OMs) were neither morphol. altered nor permeabilized to lysozyme by polymyxin B concns., although both effects were obsd. for controls. EDTA and peptides increased or accelerated the participation of the hydrophobic probe N-phenyl-naphthylamine into Escherichia coli and Haemophilus influenzae OMs but had no effect on Brucella OMs. Since Brucella and H. influenzae OMs are permeable to hydrophobic compds., the results show that such unusual permeability is not necessarily related to resistance to polycations. Although rough (R) B. abortus and B. ovis were more resistant than the controls were, there were qual. and quant. differences with smooth (S) brucellae; this may explain known host range and virulence differences. Brucella S-lipopolysaccharides (LPSs) had reduced affinities for polycations, and insertion of brucella and Salmonella montevideo S-LPSs into the OM of a Brucella R-LPS mutant increased and decreased, resp., its resistance to cationic peptides. The results show that the core lipid A of Brucella LPS plays a major role in polycation resistance and that O-chain d. also contributes significantly. It is proposed that the features described above contribute to Brucella resistance to the oxygen-independent systems of phagocytes.

L60 ANSWER 27 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:315809 HCAPLUS
DOCUMENT NUMBER: 120:315809
TITLE: Treatment of gynecological malignancies with biologically active peptides
INVENTOR(S): Jacob, Leonard S.; Maloy, W. Lee; Baker, Margaret A.
PATENT ASSIGNEE(S): Magainin Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405313	A1	19940317	WO 1993-US7798	19930816
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9350811	A1	19940329	AU 1993-50811	19930816
US 5635479	A	19970603	US 1995-434120	19950502

PRIORITY APPLN. INFO.: US 1992-937462 A 19920831
WO 1993-US7798 W 19930816
US 1994-226108 B1 19940411
US 1994-297950 B1 19940831

AB A gynecol. malignancy is treated by administering .gtoreq.1 biol. active amphiphilic peptide or protein. The peptide or protein may be administered intralesionally, i.v., or i.p., whereby the peptide or protein may inhibit, prevent, or destroy the growth of the gynecol. malignancy, such as an ovarian cancer, uterine cancer, or cervical cancer. Mice injected with murine spontaneous ovarian teratoma cells were injected with 22 mg/kg of Gly-Ile-Gly-Lys-Phe-Leu-Lys-Lys-Ala-Lys-NH2 (I) or all D-I or 130 mg/kg of **cecropin A**. The untreated mice succumbed to the tumor burden within 20 days while all the treated mice lived >70% longer.

L60 ANSWER 28 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:403055 HCAPLUS
DOCUMENT NUMBER: 119:3055
TITLE: Preparation of antimicrobial peptides and their use against plant pathogens
INVENTOR(S): Mapelli, Claudio; Dugas de Robertis, Catherine; Stahl, Geraldine Frances; Bascomb, Newell Fred; Swerdloff, Michael Dennis; Williams, Jon Ira; Everett, Nicholas Paul
PATENT ASSIGNEE(S): Istituto Guido Donegani S.p.A., Italy
SOURCE: Eur. Pat. Appl., 79 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 497366	A2	19920805	EP 1992-101616	19920131
EP 497366	A3	19940209		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9210650	A1	19920806	AU 1992-10650	19920130
AU 648140	B2	19940414		
CA 2060455	AA	19920802	CA 1992-2060455	19920131
JP 05294995	A2	19931109	JP 1992-59848	19920131
EP 919566	A2	19990602	EP 1998-121780	19920131
EP 919566	A3	19991201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5519115	A	19960521	US 1993-164151	19931209

PRIORITY APPLN. INFO.: US 1991-649784 19910201
EP 1992-101616 19920131

OTHER SOURCE(S): MARPAT 119:3055

AB Oligopeptides (19), such as **magainins** 1 and 2, **cecropin A**-NH2, **magainin** 2 dimers (head-to-tail and bridged), reverse **magainins** 1 and 2, Ser-**magainin** 2, and Met[Arg7,Glu8,de-Ser23]**magainin** 1, are useful for the control of plant-pathogenic microorganisms. Some of the peptides were prepd., using known methods. A screening method is given for detn. of the phytotoxicity of antimicrobial peptides. Some peptides were obtained by std. mol. cloning. Most peptides were effective at <10 .mu.g/mL against Fusarium, Trichoderma reesei, Cercospora, and Helminthosporium carbonum in vitro. Complementary peptide mixts. are given.

L60 ANSWER 29 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:600959 HCAPLUS
DOCUMENT NUMBER: 121:200959
TITLE: Effect of some **antibacterial** peptides on mitochondrial respiration and in vitro import of a nuclear encoded precursor protein
AUTHOR(S): Hugosson, Marie; Boman, Hans G.; Glaser, Elzbieta
CORPORATE SOURCE: Department Biochemistry, Stockholm University, Stockholm, 106 91, Swed.
SOURCE: Mol., Biochem. Physiol. Aspects Plant Respir. (1992), 367-72. Editor(s): Lambers, H.; Van der Plas, L. H. W. SPB Acad. Publ.: The Hague, Neth.
CODEN: 60FCA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Cecropins and other **antibacterial** peptides act as uncouplers of oxidative phosphorylation and these peptides affect binding and import of a nuclear-encoded , mitochondrial precursor protein.

L60 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:400767 HCAPLUS
DOCUMENT NUMBER: 115:767
TITLE: **Antibacterial** and antimalarial hybrid peptides, derived from cecropins
INVENTOR(S): Boman, Hans G.; Merrifield, Robert Bruce
PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9011771	A1	19901018	WO 1990-US2082	19900412
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
CA 2031199	AA	19901013	CA 1990-2031199	19900412
EP 422215	A1	19910417	EP 1990-908061	19900412
EP 422215	B1	19980819		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
JP 03501742	T2	19910418	JP 1990-506821	19900412
JP 07030120	B4	19950405		
AT 169824	E	19980915	AT 1990-908061	19900412

PRIORITY APPLN. INFO.: US 1989-336777 19890412
US 1989-449593 19891212
WO 1990-US2082 19900412

AB **Antibacterial** and/or antimalarial hybrid peptides, originating from **cecropins A**, B, and D, melittin, **magainin**

and attacin, contg. 20-40 amino acid residues, were prepd. by std. solid-phase techniques. Each peptide has a hydrophobic and a hydrophilic region, and most have regions of helicity and amphipathicity. Proline is often used to interrupt a helix. The hybrid **cecropin A** (1-13)melittin (1-13) was much more potent than **cecropin A** against the blood stream form of Plasmodium falciparum, as shown by the method of B. Wahlin, et al. (1984).

L60 ANSWER 31 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002232549 EMBASE
TITLE: Salt resistance and synergistic effect with vancomycin of .alpha.-helical antimicrobial peptide P18.
AUTHOR: Shin S.Y.; Yang S.-T.; Park E.J.; Eom S.H.; Song W.K.; Kim Y.; Hahm K.-S.; Kim J.I.
CORPORATE SOURCE: J.I. Kim, Department of Life Science, Kwangju Inst. of Sci. and Technology, Kwangju 500-712, Korea, Republic of. jikim@eunhasu.kjist.ac.kr
SOURCE: Biochemical and Biophysical Research Communications, (2002) 290/1 (558-562).
Refs: 32
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB P18 (KWKLFKKIPKFLHLAKKF-NH(2)) is an .alpha.-helical antimicrobial peptide designed from a **cecropin A-magainin 2** hybrid. In this study, P18 was found to show strong antimicrobial activity against several antibiotic-resistant bacterial and fungal strains. Both the salt resistance on antimicrobial activity and the synergistic effect with clinically used antibiotic agents are critical factors in developing effective peptide antibiotic drugs. For this reason, we investigated the salt resistance of P18 to antagonism by NaCl, CaCl(2), and MgCl(2) on antimicrobial activity and the synergistic effect of P18 with vancomycin against vancomycin-resistant Enterococcus faecium (VREF). Compared to **magainin 2**, P18 showed strong resistance on antimicrobial activity against bacterial strains and C. albicans under high NaCl concentrations of 100-200 mM. In addition, P18 displayed much greater salt resistance on antibacterial activity against Gram-negative bacteria at the physiological or elevated concentrations of CaCl(2) and MgCl(2) than **magainin 2**. Furthermore, the combination study revealed that P18 has a relatively effective synergistic effect with vancomycin against VREF. Thus, these results support that P18 may prove to be a salt-resistant antibiotic peptide potentially useful in the treatment of cystic fibrosis patients as well as a valuable adjuvant for antimicrobial chemotherapy. .COPYRGT. 2002 Elsevier Science.

L60 ANSWER 32 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001239427 EMBASE
TITLE: Antimicrobial peptides: A potential role in ocular therapy.
AUTHOR: Aliwarga Y.; Hume E.B.H.; Lan J.; Willcox M.D.P.
CORPORATE SOURCE: Y. Aliwarga, Coop. Res. Ctr. Eye Res./Technol., University of New South Wales, Sydney, NSW 2052, Australia. y.aliwarga@cclru.unsw.edu.au
SOURCE: Clinical and Experimental Ophthalmology, (2001) 29/3 (157-160).
Refs: 32
ISSN: 1442-6404 CODEN: CEOPBW

COUNTRY: Australia
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Bacterial pathogens are often involved in contact lens-related adverse responses. This study aimed to find antimicrobial peptides and proteins that effectively eradicate or inhibit ocular bacteria. The antimicrobials were screened against Gram-negative and Gram-positive bacteria originating from ocular sources. The viability of these ocular bacteria was measured after exposure to the peptides and proteins. Two conditions were used to grow bacteria, low nutrient phosphate-buffered saline and high nutrient tryptone soya broth. Samples were taken at different times up to 48 h. In low nutrient conditions, protamine was found to be the most effective against all strains. Melittin was very effective against all strains except Serratia and one Pseudomonas isolate which were partially affected. In high nutrient condition, only melittin was effective in killing Staphylococcus aureus. Protamine and the combination of protamine and melittin had the greatest effect in eradicating the bacteria tested in low nutrient condition. Protamine alone and its combination with melittin may have potential therapeutic agents for ocular infections in an era of emerging antibiotic resistance.

L60 ANSWER 33 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000055825 EMBASE
TITLE: Effects of the hinge region of **cecropin A** (1-8)-**magainin 2**(1-12), a synthetic antimicrobial peptide, on liposomes, bacterial and tumor cells.
AUTHOR: Shin S.Y.; Kang J.H.; Jang S.Y.; Kim Y.; Kim K.L.; Hahm K.-S.
CORPORATE SOURCE: K.S. Hahm, Peptide Engineering Research Unit, Research Institute of Bioscience, P.O. Box 115, Yusong, Taejon 305-600, Korea, Republic of. hahmks@kribb4680.kribb.re.kr
SOURCE: Biochimica et Biophysica Acta - Biomembranes, (2000) 1463/2 (209-218).
Refs: 41
ISSN: 0005-2736 CODEN: BBBMBS
PUBLISHER IDENT.: S 0005-2736(99)00210-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A 20-residue hybrid peptide (CA(1-8)-MA(1-12): KWKLFKKIGIGKFLHSAKKF-NH2) incorporating 1-8 residues of **cecropin A** (CA) and 1-12 residues of **magainin 2** (MA) has potent antibiotic activity without hemolytic activity. In order to investigate the effects of the flexible hinge sequence, Gly-Ile-Gly of CA(1-8)-MA(1-12) (CA-MA) on antibiotic activity, CA-MA and its three analogues, CA-MA1, CA-MA2 and CA-MA3 were synthesized. The Gly-Ile-Gly sequence of CA-MA was deleted in CA-MA1 and replaced with Pro and Gly-Pro-Gly in CA-MA2 and CA-MA3, respectively. CA-MA1 and CA-MA3 caused a significant decrease in the bactericidal rate against Escherichia coli and Bacillus subtilis and the tumoricidal activity against four different tumor cells, and the PC/PS (4:1, w/w) vesicle-aggregating and disrupting activities. However, CA-MA2

showed a similar bactericidal rate and antitumor, vesicle-aggregating and disrupting activities, as compared with CA-MA. These results suggested that the flexibility or .beta.-turn induced by Gly-Ile-Gly or Pro in the central part of CA-MA may be important in the electrostatic interaction of the cationic short .alpha.-helical region in the N-terminus with the cell membrane surface and the hydrophobic interaction of amphipathic .alpha.-helical region in the C-terminus with the hydrophobic acyl chains in the cell membrane. CA-MA3 exhibited lower activity in antibacterial, antitumor, and vesicle-aggregating and disrupting activities than CA-MA and CA-MA2. This result suggested that the excessive .beta.-turn structure by Gly-Pro-Gly in CA-MA3 seems to interrupt the ion channel/pore formation on the lipid bilayer. It was concluded that the appropriate flexibility or .beta.-turn structure provided by the central hinge is responsible for the effective antibiotic activity of the antimicrobial peptides with the helix-hinge-helix structure. Copyright (C) 2000 Elsevier Science B.V.

L60 ANSWER 34 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999216784 EMBASE
TITLE: NMR structural characterization of **cecropin A**(1-8) - **magainin 2**(1-12) and **cecropin A**(1-8) - melittin(1-12) hybrid peptides.
AUTHOR: Oh D.; Shin S.Y.; Kang J.H.; Hahm K.-S.; Kim K.L.; Kim Y.
CORPORATE SOURCE: Y. Kim, Department of Chemistry, Konkuk University, Kwangjin-ku, Mojin-dong 93-1, Seoul 143-701, Korea, Republic of. ymkim@kkucc.konkuk.ac.kr
SOURCE: Journal of Peptide Research, (1999) 53/5 (578-589). Refs: 41
ISSN: 1397-002X CODEN: JPERFA
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In order to elucidate the structure-**antibiotic** activity relationships of the peptides, the three-dimensional structures of two hybrid peptides, CA(1- 8) - MA(1-12) and CA(1-8) - ME(1-12) in trifluoroethanol-containing aqueous solution were investigated by NMR spectroscopy. Both CA(1-8) - MA(1-12) and CA(1-8) - ME(1-12) have strong antibacterial activity but only CA(1-8) - ME(1-12) has hemolytic activity against human erythrocytes. CA(1-8) - MA(1- 12) has a hydrophobic 310-helix of only two turns combined with one short helix in the N-terminus with a flexible hinge section in between. CA(1-8) - MA(1-12) has a severely bent structure in the middle of the peptide. These structural features as well as the low hydrophobicity of CA(1-8) - MA(1-12) seem to be crucial for the selective lysis against the membrane of prokaryotic cells. CA(1-8) - ME(1-12) has an .alpha.-helical structure of about three turns in the melittin domain and a flexible structure with one turn in the cecropin domain connected with a flexible hinge section in between, and these might be the structural features required for membrane distruption against prokaryotic and eukaryotic cells. The central hinge region (Gly9- Ile10-Gly11) in an amphipathic antibacterial peptide is considered to play an important role in providing the conformational flexibility required for ion channel formation of the C-terminal hydrophobic .alpha.-helix on cell membrane.

L60 ANSWER 35 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999052051 EMBASE
TITLE: Structure-antifungal activity relationships of cecropin A-magainin 2 and cecropin A-melittin hybrid peptides on

pathogenic fungal cells.
AUTHOR: Dong Gun Lee; Zhe Zhu Jin; Song Yub Shin; Joo Hyun Kang; Hahm K.-S.; Kil Lyong Kim
CORPORATE SOURCE: K.L. Kim, Peptide Engineering Research Unit, Korea Res. Inst. Biosci./Biotechnol., KIST, P.O. Box 115, Yusong, Taejon 305-600, Korea, Republic of. kimkl@kribb4680.kribb.re.kr
SOURCE: Journal of Microbiology and Biotechnology, (1998) 8/6 (595-600).
Refs: 18
ISSN: 1017-7825 CODEN: JOMBES
COUNTRY: Korea, Republic of
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In order to investigate a relationship of the structure-antifungal and hemolytic activities between cecropin A(1-8)magainin 2(1-12) and cecropin A(1-8)-melittin(1-12) hybrid peptides, several analogues with amino acid substitution at positions 10 (Ile) and 16 (Ser) were designed and synthesized. The increase of the hydrophobicity by substituting with Leu, Phe, and Trp at position 16 in cecropin A(1-8)-magainin 2(1-12) did not have a significant effect on antifungal activity but caused a remarkable increase in hemolytic activity. These results indicate that the hydrophobic property at position 16 of cecropin A(1-8)-magainin 2(1-12) is more correlated to hemolytic activity than to antifungal activity. Replacement with Pro at position 10 of cecropin A(1-8)magainin 2(1-12) and cecropin A(1-8)-melittin (1-12) caused a remarkable decrease in .alpha.-helical contents in the 50% TFE solution and induced a reduction in lyric activity against Aspergillus flavus, and Aspergillus fumigatus. These results demonstrate that flexibility at the central hinge region is essential for lyric activity against fungal cells and .alpha.-helicity of the peptides.

L60 ANSWER 36 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90010301 EMBASE
DOCUMENT NUMBER: 1990010301
TITLE: Antibacterial and antimalarial properties of peptides that are cecropin-melittin hybrids.
AUTHOR: Boman H.G.; Wade D.; Boman I.A.; Wahlin B.; Merrifield R.B.
CORPORATE SOURCE: Departmant of Microbiology, University of Stockholm,S-10691 Stockholm, Sweden
SOURCE: FEBS Letters, (1989) 259/1 (103-106).
ISSN: 0014-5793 CODEN: FEBLAL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Solid phase synthesis was used to produce 5 hybrid peptides containing sequences from the antibacterial peptide, **cecropin A**, and from the bee venom toxin, melittin. Four of these chimeric peptides showed good antibacterial activity against representative Gram-negative and Gram-positive bacterial species. The best hybrid, **cecropin A**(1-13)-melittin(1-13) was 100-fold more active than **cecropin A** against Staphylococcus aureus. It was also a 10-fold better antimalarial agent than cecropin B or **magainin 2**. Sheep red cells were lysed by melittin at low concentrations, but not by the hybrid molecules, even at 50 times higher concentrations.

L60 ANSWER 37 OF 39 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-248282 [24] WPIX
DOC. NO. CPI: C2003-064111
TITLE: New peptide based on **cecropin** and magainin, useful e.g. for treatment or prevention of metabolic bone disease, inhibits osteoclast differentiation.
DERWENT CLASS: B04 D21
INVENTOR(S): HAHM, K; KIM, H; LEE, Z
PATENT ASSIGNEE(S): (KOME-N) KOMED CO LTD
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003014146	A1	20030220	(200324)*	EN	54

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003014146	A1	WO 2002-KR1508	20020807

PRIORITY APPLN. INFO: KR 2001-47541 20010807
AB WO2003014146 A UPAB: 20030410
NOVELTY - Peptide (I) that inhibits osteoclast differentiation with a sequence of at least 70% homologous with peptide P1 of formula Lys-Tyr-Lys-Phe-(Lys)2-Ile-Pro-Lys-Phe-Leu-His-Leu-Ala-(Lys)2-Phe, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) A peptide P1;
(2) Nucleic acid (II) that encodes P1; and
(3) Method for preparing (I).
ACTIVITY - Osteopathic; Cytostatic; Antiarthritic; Antirheumatic.
Bone marrow cells and osteoclasts, both from ICR mice, were co-cultured for 6 days, then fixed, stained by the tartrate-resistant acid phosphatase method and stained osteoclasts counted. At a concentration of 20 nM, P1 prevented development of any osteoclasts. In a P1-free control the mean numbers of such cells were 314, mononucleated, and 158, multinucleated; and in presence of 2 nM P1 the corresponding figures were 175 and 83.
MECHANISM OF ACTION - None given in the source material.
USE - (I) Are used for treatment and prevention of metabolic bone diseases, particularly metastatic lesions to bone from breast or prostatic carcinoma; primary bone tumors (e.g. multiple myeloma); rheumatoid or degenerative arthritis; periodontal diseases where alveolar bone is destroyed by bacteria; inflammatory bone resorption caused by dental implants or implants in orthopedic surgery, and genetic Paget's disease (all claimed), also osteoporosis (not claimed). (I) can also be used, in slow release formulations or as coatings on dental implants, for treating periodontal disease, or they are included in toothpastes and mouthwashes.

ADVANTAGE - Compared with known compounds, (I) are more active with fewer side effects, especially they are not toxic to osteoblasts, bone marrow or other cells.
Dwg.0/10

L60 ANSWER 38 OF 39 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-206179 [26] WPIX
DOC. NO. CPI: C2002-063210
TITLE: Novel modified biological peptide with increased biological potency, prolonged activity, increased half-life, for treating glucose intolerance associated or not with insulin resistance pathologies, type II diabetes.
DERWENT CLASS: B04 B05
INVENTOR(S): ABRIBAT, T; GRAVEL, D; HABI, A
PATENT ASSIGNEE(S): (THER-N) THERATECHNOLOGIES INC
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002010195	A2	20020207	(200226)*	EN	77

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001079526	A	20020213	(200238)	
EP 1305338	A2	20030502	(200331)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002010195	A2	WO 2001-CA1119	20010802
AU 2001079526	A	AU 2001-79526	20010802
EP 1305338	A2	EP 2001-957662	20010802
		WO 2001-CA1119	20010802

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001079526	A	Based on	WO 200210195
EP 1305338	A2	Based on	WO 200210195

PRIORITY APPLN. INFO: US 2000-222619P 20000802
AB WO 200210195 A UPAB: 20020424
NOVELTY - A modified biological peptide (I) with increased biological potency, prolonged activity and/or increased half-life, and any isomers, including cis and trans configurations, epimers, enantiomers, diastereoisomers, and racemic mixtures, where the peptides defined in claim 1 of US 6020311 is excluded, is new.
DETAILED DESCRIPTION - A modified biological peptide of formula Xn-R1 (I) with increased biological potency, prolonged activity and/or increased half-life, and any isomers, including cis and trans configurations, epimers, enantiomers, diastereoisomers, and racemic mixtures, where the peptides defined in claim 1 of US 6020311 is excluded, is new.

R1 = a peptide sequence, a functional analog or its fragment;
X = identical or independent from the others, is constituted by conformationally rigid moieties, and is selected from straight, substituted (1-10)C alkyl, a branched, substituted (1-10)C alkyl, a straight or branched, unsubstituted or substituted (1-10)C alkene, a straight or branched, unsubstituted or substituted (1-10)C alkyne, an unsubstituted or substituted saturated or unsaturated (3-10)C cycloalkyl or heterocycloalkyl where the heteroatom is O, S or N, and an unsubstituted or substituted (5-14)C aryl or heteroaryl where the heteroatom is O, S or N, where the substituents comprise one or more straight or branched (1-10)C alkyl, straight or branched (1-6)C alkene, straight or branched (1-6)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl where at least 2 carbon atoms are optionally connected to the (1-10)C alkyl, (1-10)C alkene, (1-10)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl, and (5-14)C aryl or heteroaryl, or (5-14)C aryl or heteroaryl where at least 2 carbon atoms of the aryl or heteroaryl are optionally connected to the (1-10)C alkyl, (1-10)C alkene, (1-10)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl, and (5-14)C aryl or heteroaryl, or X also comprises at least one group selected from a carboxy or an amino group for coupling with the peptide sequence by an amide bond at the N-terminal of the peptide sequence, the C-terminal of the peptide sequence, at an available carboxy or amino site on the peptide sequence chain and their combinations, and a carboxy group for coupling with the peptide sequence by an ester bond at an available hydroxy site on the peptide sequence chain, and their combinations; and
n = 1-5.

ACTIVITY - Antidiabetic; Osteopathic; Cytostatic; Antiinflammatory; Anorectic; Nootropic.

Six-week old female CDI mice were fasted for at least 16 hours. Mice were given 1.5 mg of glucose/g of body weight orally in water through a gastric gavage tube and blood was collected from a tail vein for measurement of blood glucose using a glucose meter. Peptides or vehicle were injected subcutaneously 5 minutes prior to the glucose administration. All peptides, including wild-type glucagon-like peptide GLP-1 (7-37), were tested at different concentrations: 1, 5 and 10 micro g/mouse. In a first set of experiments, a peptide 1 ((hexenoyl-trans-3-His7)-hGLP-1 (7-37)) was tested in comparison with vehicle and hGLP-1 (7-37). In a second set of experiments, peptides 2 ((O-Tolylacetic acid-His7)-hGLP-1 (7-37)) and 3 ((+/-)-cis-2-ethylcyclopropylacetic acid-His7)-hGLP-1 (7-37)) were tested in comparison with vehicle and hGLP-1 (7-37). In the two studies, administration of vehicle resulted in a similar integrated response in glucose levels. Although GLP-1 induced a dose-related decrease in the glucose response, this peptide was not able to completely suppress the glucose response at any dose, which was interpreted as a limitation in its potential clinical usefulness. In contrast, peptide 1 completely abolished the glucose response, but only at the 10 micro g dose. Surprisingly, peptide 3 was even more potent than peptide 1, and totally prevented the glucose response both at the 5 micro g and the 10 micro g doses. In conclusion, the GPL-1 analog corresponding to peptide 3 was identified with marked increased biological potency over the wild type GLP-1 (7-37), and because of this increased potency, this peptide had clinical usefulness in treating states of insulin resistance associated with pathologies such as type II diabetes.

MECHANISM OF ACTION - Blood glucose regulator; enhancer of mucosal regeneration in patients with intestinal diseases; regulator of myometrial contractility and prostoglandin release; stimulator of ACTH release; inhibitor of interleukin-8 production; stimulator of acid release; modulator of melanocyte information process, involved in pressure and volume homeostasis; regulator of exocrine and endocrine secretions, smooth muscle contraction, feeding, blood pressure, blood glucose, body temperature, cell growth, food intake and energy balance; inhibitor of

cancer cell growth; stimulator of pancreatic secretion or cell growth.
USE - (I) Is useful in the treatment of glucose intolerance associated or not with insulin resistance pathologies, and in the treatment of type II diabetes (claimed). (I) Is useful for treating bone diseases such as osteoporosis, cancer, diseases related to inflammatory responses, obesity, autism, pervasive developmental disorders, hyperproliferative skin diseases, hormone-dependent diseases and conditions including hormone-dependent cancers, for regulating blood glucose, to enhance mucosal regeneration in patients with intestinal diseases, for altering the proliferation of peripheral blood mononuclear cell, regulation of myometrial contractility and prostoglandin release, stimulation of ACTH release, inhibition of interleukin-8 production, stimulation of acid release, modulation of melanocyte information process, involved in pressure and volume homeostasis, regulation of exocrine and endocrine secretions, smooth muscle contraction, feeding, blood pressure, blood glucose, body temperature and cell growth, regulation of food intake and energy balance, inhibition of cancer cell growth and stimulation of pancreatic secretion or cell growth.
ADVANTAGE - (I) Is a modified biological peptide and has increased biological potency, prolonged activity and/or increased half-life (claimed).
Dwg.0/2

L60 ANSWER 39 OF 39 WPIX (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1991-281214 [38] WPIX
DOC. NO. CPI: C1991-151788
TITLE: Compsns. for treating infections sensitive to beta-lactam antibiotics - comprise beta-lactam antibiotic and cationic oligopeptide, useful against Enterobacteriaceae, Pseudomonas aeruginosa etc..
DERWENT CLASS: B02 B04
INVENTOR(S): BLAKE, J J; COSAND, W L; DARVEAU, R P; COSAND, W J; DARVEAU, R C
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 29
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9112815	A	19910905	(199138)*		
RW: AT BE CH DE DK ES FR GB IT LU NL					
W: AU CA FI HU JP KR NO SU					
PT 96859	A	19911031	(199148)		
AU 9174856	A	19910918	(199150)		
ZA 9101347	A	19911127	(199202)		
CN 1054900	A	19911002	(199227)		
FI 9203747	A	19920820	(199247)		
EP 516747	A1	19921209	(199250)	EN	70
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NO 9203298	A	19921021	(199305)		
CZ 9100477	A3	19930414	(199331)		
HU 63567	T	19930928	(199344)		
JP 05506645	W	19930930	(199344)		25
NZ 237202	A	19940126	(199407)		
AU 650262	B	19940616	(199429)		
US 5409898	A	19950425	(199522)		24
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PT 96859	A		PT 1991-96859	19910222
ZA 9101347	A		ZA 1991-1347	19910225
CN 1054900	A		CN 1991-102223	19910223
FI 9203747	A		WO 1991-US1224	19910225
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EP 516747	A1		EP 1991-905923	19910225
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NO 9203298	A		WO 1991-US1224	19910225
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CZ 9100477	A3		CS 1991-477	19910225
HU 63567	T		WO 1991-US1224	19910225
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JP 05506645	W		JP 1991-506018	19910225
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NZ 237202	A		NZ 1991-237202	19910222
AU 650262	B		AU 1991-74856	19910225
US 5409898	A	CIP of	US 1990-484020	19900223
		Cont of	US 1991-655321	19910219
			US 1994-233203	19940426
EP 516747	A4		EP 1991-905923	
IL 97344	A		IL 1991-97344	19910224

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PATENT NO	KIND		PATENT NO
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The composition comprises beta-lactam antibiotic which can inhibit growth of the organism and a cationic oligopeptide. The antibiotic is a penicillin, a cephalosporin, a carbapenem, (especially impinenem), a monobactam, (especially aztreonam) a cephamycin, a pyrazidone or a penem, and the cationic oligopeptide is a magainin, a **cecropin**, a sarcotoxin, or mitochondrial precursor protein. The cationic oligopeptide can also be e.g. human platelet factor-4 or its fragment, analogue or derivative. The human platelet factor-4 is a C-13 peptide with the sequence

Pro-Ley-Tyr-Lys-Ile-Lys-Lys-Leu-Leu-Glu-Ser

USE/ADVANTAGE - The beta-lactam antibiotic and the cationic oligopeptide act synergistically for treatment of bacterial infections especially by Enterobacteriaceae bacteria. Infection caused by E. coli, Pseudomonas aeruginosa, Enterobacter clocae and Klebsiella pneumoniae can be especially by administering cefepime and **magainin 2**. Administration can be systemic, topical or local.

In an example, neutropenic mice were challenged with 20000 E. coli and divided into four groups. Their survival was monitored over 10 days. In the group administered **magainin 2** and cafepime 11 out of 20 mice survived compared to 1 out of 15 for the control. @(70pp Dwg.No.0/8

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